ITEM 2:

NON-TECHNICAL ABSTRACT

Epstein-Barr virus (EBV) and cytomegalovirus (CMV) usually do not cause fatal disease in normal individuals. However, patients receiving certain types of bone marrow transplants, such as stem cells depleted of T-cells, may be susceptible to aggravated EBV and/or CMV disease, in the form of tumors (lymphoma) for the former, and infection (pneumonia/hepatitis) for the latter. Although medicine is effective against EBV/CMV diseases, these drugs often have severe side-effects, and as a result cannot be used in some individuals.

Adoptive immunotherapy is a new approach of treating/preventing EBV/CMV diseases. It involves growing virus-recognizing T-cells in the laboratory, and then infusing the T-cells into patients. T-cells are the major defense against infections of viruses, including CMV and EBV. Immunotherapy against EBV disease has been successfully applied in some medical centers. It uses the EBV-infected B-cells to stimulate the growth of T-cells. In contrast, immunotherapy for CMV disease, which calls for CMV-infected fibroblasts as stimulators, is less accepted because of several problems, including the long time needed to produce the T-cells, the inconvenience of taking skin biopsies from donors, and the requirements for special media to grow the cells.

Our laboratory has developed a novel system to grow T-cells that recognize both EBV and CMV simultaneously. To achieve this goal, the EBV-infected B-cells are engineered to make a CMV protein pp65, a known potent viral antigen. A recombinant retrovirus MSCVpp65 is used to deliver the pp65 gene into the B-cells, and the pp65 gene becomes one integral part of the genes of these B-cells. Thus, the same B-cells would stimulate the growth of both EBV- and CMV-recognizing T-cells. Data from experiments confirmed that the T-cells stimulated by the engineered B-cells can kill EBV- and CMV-infected cells.

We plan to infuse donor-derived T-cells into recipients of stem cell transplants, who meet study criteria and voluntarily consent. Infusion will take place at 40, 60 and 80 days after transplantation. T-cell cultures will be analyzed for effectiveness and tested for contaminants. Only qualified products will be used for infusion. Patients who receive the T-cells will also be tested to evaluate the effectiveness of the therapy and possible side-effects after receiving the T-cell infusion. The tests include measuring 1) EBV DNA and CMV antigens in the blood, and 2) the number of T-cells that recognize EBV and CMV. Patients also will be tested for any potential risk of being exposed to contaminants. Patients will be informed of any progress of the immunotherapy, and the scientific data obtained will be shared among the medical community.